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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/663,885	09/15/2000	Jeannette Whitcomb	2793/63122/JPW/JML/CMR	3908

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EXAMINER	
PARKIN, JEFFREY S	
ART UNIT	PAPER NUMBER
1648	9

DATE MAILED: 02/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/663,885	WHITCOMB, JEANNETTE	
	Examin r	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *10-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Office Action

Status of the Claims

1. Applicant's election with traverse of Group I (claims 1-9) in paper no. 9 is acknowledged. The traversal is based upon the argument that the inventions of Groups I-III are not "independent" since they relate to common subject matter. Applicant further maintains that it would not be a serious burden on the examiner if all the groups were searched concomitantly. These arguments are not deemed to be persuasive for the reasons of record previously set forth in paper no. 6. Applicant is reminded that establishment of *prima facie* evidence for a serious burden requires the demonstration, by appropriate explanation, of either separate classification, separate status in the art, or a different field of search as defined in M.P.E.P. § 808.02. The following items adduce a *prima facie* showing of burden: 1) The inventions of Groups I-III all display a separate classifications and a separate status in the art. 2) The inventions of Groups I-III are all directed towards independent and distinct inventions as previously set forth in paper no. 6. The reasons for this determination were set forth as follows:

> 2. The inventions are distinct, each from the other because of the following reasons:
>
> 3. Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (M.P.E.P. § 806.04 and § 808.01). In the instant case, each of the identified groups is directed toward a different scientific objective (i.e., determining a patient prognosis, identifying putative antiviral candidate compounds) that employ structurally and functionally different scientific reagents and assays steps. Therefore, each group is clearly directed toward a different inventive concept.
>
> 4. Inventions I and III are unrelated. Inventions are

unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (M.P.E.P. § 806.04 and § 808.01). In the instant case, the methodology of Group I neither requires nor uses the product of Group III. Accordingly, each group is directed toward a different inventive entity.

5. Inventions II and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case, the nucleic acid of Group III can be employed in a number of materially different processes such as protein expression assays or nucleic acid-based HIV allelic screening assays.

6. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, recognized divergent subject matter, and require separate searches, restriction for examination purposes as indicated is proper.

Accordingly, each invention will generate unique issues regarding novelty, patentability, and enablement. 3) Since the inventions disclosed *supra* are directed towards patentably distinct material, a search for one invention would not necessarily result in the identification of art that is concomitant with that required to address the issues generated by the other inventions. Accordingly, the **requirement is still deemed to be proper and is therefore made FINAL.** Claims 10-17 are withdrawn from further consideration by the examiner, pursuant to 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

Information Disclosure Statement

2. The information disclosure statement filed 19 August, 2002, has been placed in the application file and the information referred to therein has been considered.

35 U.S.C. § 112, Second Paragraph

3. Claims 1-9 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims reference a "mutation at codon 66" that correlates with a certain non-nucleoside reverse transcriptase inhibitor (NNRTI) phenotype which is vague and indefinite because the claims fail to identify the mutation(s) that correlates with the desired phenotype. What is the precise mutation that is being detected? For instance, do susceptible strains display a change from alanine to isoleucine. Moreover, the claims also reference an HIV integrase and HIV-infected patient. However, perusal of the specification appears to demonstrate that mutations in the HIV-1 IN are being assessed, not HIV-2. Clearly setting forth the virus (e.g., HIV-1 or HIV-2) and codon (e.g., 66) are important to understanding the invention, particularly in light of the genotypic/phenotypic heterogeneity between HIV-1 and -2. Absent further clarification and amendment of the claim language, the metes and bounds of the patent protection desired cannot be ascertained.

4. Claims 1-4 and 9 are vague and indefinite for referencing a method of assessing NNRTI phenotype susceptibility by measuring changes in the HIV-1 integrase. NNRTIs are non-nucleoside **reverse transcriptase inhibitors** (e.g., delavirdine, nevirapine, and efavirenz) that target the HIV-1 reverse transcriptase (RT), **not** the integrase (IN). Thus, it is not readily manifest how the detection of a genotypic change in the IN would correlate to an RT phenotype. Appropriate correction is required.

35 U.S.C. § 112, First Paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C.

§ 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-4 and 9 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed toward a method of assessing the effectiveness of NNRTI therapy in an HIV-infected patient by measuring genotypic changes in the IN, wherein said changes correlate with increased susceptibilities to delavirdine, neveriapine, and efavirenz. The claims are not enabled because the disclosure fails to provide a correlation between NNRTI-resistance and genotypic changes in the IN. NNRTIs are specific inhibitors of the HIV-1 reverse transcriptase. They do not target the IN but are specific for the RT. Thus, genotypic changes in the IN would not be expected to correlate with NNRTI-drug susceptibility. Accordingly, the skilled artisan could not practice the invention as currently claimed.

7. Claims 5-8 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The claims are broadly directed toward phenotypic screening methods by assessing the presence or absence of a mutation at codon 66 of the HIV IN. Appropriately drafted claim language that clearly sets forth the HIV-1 IN mutation being detected would be acceptable (i.e., a method of assessing ...

detecting a mutation in the HIV-1 IN consisting of S66I ...).

The legal considerations that govern enablement determinations pertaining to undue experimentation are disclosed in *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988) and *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The disclosure fails to identify those mutations that correlate with the desired phenotype. The claims only specify that a mutation at codon 66 is detected. However, it fails to provide a clear correlation between any given genotypic change and the corresponding phenotype. Thus, the skilled artisan has been asked to guess as to which amino acid substitutions are permissible.

2) The claims are of considerable breadth and encompass a large genus of mutations. However, the disclosure fails to provide any guidance pertaining to those mutations and their relevance to the phenotype of interest.

3) The art is unpredictable thereby precluding the skilled artisan from ascertaining which genotypic changes in IN correspond to the appropriate phenotype.

Thus, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

Correspondence

8. Correspondence related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Official communications should be directed toward one of the following Group 1600 fax numbers: (703) 308-4242 or (703) 305-3014. Informal communications may be submitted directly to the Examiner through the following fax number: (703) 308-4426. Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.

9. Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (703) 308-2227. The examiner can normally be reached Monday through Thursday from 8:30 AM to 6:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisors, James Housel or Laurie Scheiner, can be reached at (703) 308-4027 or (703) 308-1122, respectively. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

23 February, 2003